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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/358,788	07/22/1999	MICHAEL J. HELLER	0031/81494/JPW/GC	1976

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EXAMINER	
FORMAN, BETTY J	
ART UNIT	**PAPER NUMBER**
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/358,788	HELLER ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *49,57,58 and 79-81* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *49,57,58 and 79-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

Status of the Claims

1. This action is in response to papers filed 2 December 2010 in which claim 49 was amended and the previous rejections were traversed.

The amendments have been thoroughly reviewed and entered.

The previous rejections in the Office Action dated 2 September 2010 are maintained.

Applicant's arguments have been thoroughly reviewed and are discussed below.

Claims 49, 57-58 and 79-81 are under prosecution.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 49, 57, 58 and 79-81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hollis et al (U.S. Patent No. 5,846,708, filed 23 April 1992) and Cozzette et al (U.S. Patent No. 5,063,081, issued 5 November 1991).

Regarding Claims 49 and 79-81, Hollis teaches a method for analyzing a sample oligonucleotide, the method comprising forming a plurality of test sites on a substrate

(Column 4, lines 32-45, Fig. 1,4) wherein each test site is electronically addressable (Column 5, lines 6-18). Hollis further defines the electrodes in microns (Column 6, lines 1-5) thereby providing microelectrodes as claimed.

Hollis teaches electronically immobilizing oligonucleotide anchor sequences to individually selected locations (Column 13, lines 8-63), contacting the sample oligonucleotide with the immobilized probe for hybridization and subjecting the hybrids to a reverse bias potential to remove unbound oligonucleotides (Column 13, line 64-Column 14, line 19) and detecting hybridization (Column 4, lines 46-67).

Hollis further teaches facilitating hybridization by addressable application of electrical potential (Column 13, line 62-Column 14, line 26).

> The **electrically addressable test site** array of the invention also provides the ability to electronically induce or catalyze a synthesis reaction **in a given well**, or row, or column of wells, by **applying an electrical potential to the electrodes of such well** or wells.
>
> The potential can be used to attract chemical reactants from solutions disposed near the wells and/or to catalyze a specific chemical reaction in the wells.
>
> Furthermore, the hybridization between target molecular structures and completed probes can be enhanced by the application of an electrical potential to the electrodes just after the target solution is applied to the test sites. Without the application of a potential, the target molecular structures must diffuse through the solution to the probes. Due to the inefficiency of such a diffusion process, one must allow typically 1.5 to 2 hours for significant hybridization to take place, and even then a substantial number of probes remain unhybridized. An **electrical potential can draw charged target structures directly to probes near to or attached to the electrodes,** increasing both the rate of hybridization and the total number of target/probe hybridizations that can be conveniently produced in a given experiment. **Conversely, a reverse biased potential can be subsequently applied to aid in the washing (removal) of unhybridized and mismatched target molecules**. This technique is not only applicable to the electronic genosensors of FIGS. 1 through 9, which have electrodes present within each test site, but can be employed in both the micromechanical-resonator and CCD-based approaches by either using the electrodes present within or

under each test site or fabricating one or more additional electrodes at each test site for this purpose.(emphasis added)

Hollis specifically teaches addressable application of electrical potential to “draw charged target” to the electrodes. Hollis further teaches that the same method is used to in an opposite manner ("Conversely") to remove unhybridized and mismatched targets. Hence, targets are removed at selected locations as claimed.

Hollis teaches the probes are attached to the test sites directly or by fixation to a substrate e.g. attachment/glue layer (Column 11, lines 1-20 and Column 13, lines 14-20) thereby providing an attachment layer. But Hollis does not teach a selectively permeable layer in addition to the attachment layer. However, selectively permeable layers (permselective) between electrodes and the attachment layer were well known in the art at the time the invention was made as taught by Cozzette (Abstract).

Cozzette teaches a method similar to that of Hollis comprising immobilizing a binding partner (e.g. DNA) onto one of a plurality of electrodes, contacting with the complementary binding partner and detecting the interaction (Column 52, lines 4-20). Cozzette further teaches the method includes adding a probe complementary to a portion of the target that is not hybridized to the immobilized probe in a sandwich format and detecting formation of the sandwich (Column 52, lines 11-15).

Cozzette also teaches that the permselective layer also acts as an adhesion promoter for the attachment layer thereby facilitating biomolecule immobilization (paragraph spanning columns 13-14). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the permselective

and attachment layers of Cozzette to the electrodes of Hollis. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success based on the teachings of Cozzette. The artisan would have been further motivated to do so for the expected benefits of providing a barrier against interfering ionic species while allowing transport of smaller detectable moieties of interest and facilitating biomolecule immobilization as desired in the art (Cozzette, paragraph spanning columns 13-14).

Cozzette further teaches that the electrode has a permselective layer and attachment layer made from aminoproplytriethoxy silane (§ 5.1.2) and teaches that the layer acts as a barrier against interfering ionic species while allowing "effective diffusion of molecules having a molecular weight of about 50 or less" (Column 30, lines 35-40).

Diffusion of the molecules requires that the molecules be in solution. Therefore, the permselective layer of Cozzette provides the electrodes with access to solvent molecules. While the reference does not teach 5-25% of the electrode surface is accessible, it would have been obvious to one of ordinary skill in the art to optimize the permeability to provide the desired electrode access.

It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation. Absent evidence to the contrary, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to optimize the permeability of the permselective layer of Cozzette to thereby maximize the layer for interaction with the electrode/detection surface.

Regarding Claim 57, Hollis teaches the method further comprising subjecting the oligonucleotide to a field to attract it to the immobilized probe (Column 14, lines 6-14).

Regarding Claim 58, Hollis teaches the method wherein the probe is 6 to 100 bases (Example 1, Column 16, line 10).

Response to Arguments

4. Applicant argues that Hollis teaches that expose of the electrode to aqueous solutions is not desired. To support the argument Applicant cites Column 9, lines 24-27 of Hollis.

The argument and citation are noted, however the cited passage merely describes one embodiment wherein exposure of a CCD device to aqueous solutions is undesired (see Fig. 15). The passage does not exclude contact between solvents and the electrodes as claimed. Therefore the passage is not relevant to the invention as claimed. Furthermore, Hollis specifically teaches and illustrates contact between the electrodes and solvent (see Fig. 4 and accompanying text). Hollis does not teach a selectively permeable layer adjacent to the electrode and attachment layer.

However, as discussed above Cozzette teaches this element and reasoning for providing the layer to sensing electrodes.

Applicant acknowledges that Cozzette teaches a permselective layer but argues that the reference does not teach the extent to which an electrode surface is contacted by the solvent. Applicant asserts that the Cozzette teaches away from the claimed

electrode-solvent exposure because the reference teaches that the gas permeable membrane insulated the electrode from external fluid turbulence

The argument is not found persuasive. The fact that the reference teaches that the permselective layer insulates the electrode from external fluid turbulence does not alter the fact that the reference specifically teaches the layer provides for diffusion of small molecules to the electrode. Cozzette teaches that the layer allows "effective diffusion of molecules having a molecular weight of about 50 or less" thus providing contact of the molecules to the electrode (Column 30, lines 29-48).

Diffusion of the molecules requires that the molecules be in solution. Therefore, diffusion through the permselective layer of Cozzette provides the electrodes with access to solvent molecules. Thus in contrast to Applicant's assertion, Cozzette specifically teaches a permeation layer having selective diffusion properties. While the reference does not teach 5-25% of the electrode surface is accessible, it would have been obvious to one of ordinary skill in the art to optimize the permeability to provide the desired electrode access.

It is maintained that the instantly claimed method is an obvious variation of the Hollis and Cozzette methods.

Conclusion

5. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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